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HERBAL INTERVENTIONS IN MANAGING DIABETES MELLITUS: A REVIEW

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Abstract

Recent years, an exponential growth has been recorded in medicine field regarding the use of plants and their parts, and this growth is achieving acceptance both in developed countries and developing because of nature, availability and having no ill effects. The profiles accessible comprise evidence about the family name and scientific, name of plant part to be used and along with test model, hypoglycemic activity degree, and the dynamic mediators (chemical nature). Diabetes mellitus has been received the highest importance now a days and being the utmost non-communicable disease has affected people worldwide. The large numbers of plants species are revealed in current review clearly confirm the importance of herbal plants in diabetes treatment. The influence of such plants may delay the advancement of diabetic complications and precise related metabolic abnormalities. Further evaluations of bioactive chemical present in these types, can describe their hypoglycemic probable activity.

Keywords: Diabetes, complications, plants, bioactive compounds, hypoglycemic activity.

Introduction

Diabetes mellitus is such a metabolic syndrome in which long-lasting hyperglycemic condition is accompanied with relative or complete deficiency of insulin activity or its secretion (Ramadas *et al.,* 2011, Usman *et al.,* 2019, Kehinde and Sharma, 2019 and Md. A and Chitkara, 2018). The number of diabetic patients has been increased from 31.7 million in 2000 to 69.1 million in 2016 and the rise in the diabetic populations by 117% in India has declared India as "Diabetic Capital" of the world (Kumar *et al.,* 2018). According to International Diabetes Federation (IDF) the mortality rate due to diabetes has estimated globally is 281 million in men and 317 million in women (Manu and Saravanan, 2019 and Kumar *et al.,* 2019; Kumar, P., Dwivedi, P. (2018a); Kumar, P., Kumar S. *et al*. (2018b), Kumar, P., Misao, L., *et al*., 2018c, Kumar P, Dwivedi, P. 2018d, Kumar, P. and Purnima *et al*., 2018e, Kumar, P. Pathak, S. 2019f, Kumar, P. Siddique, A. *et al*., 2019g). Out of various forms Type 2 diabetes, the frequent occurring disease form present worldwide, has now extended to maximum parts of the world; rapidly spreading in various developing countries at great pace (WHO, 2006, Siddique, A. Kumar, P. 2018h, Siddique, A., Kandpal, G., Kumar P. 2018i, Pathak, S., Kumar, P., P.K Mishra, M. Kumar, M. 2017j, Prakash, A., P. Kumar, 2017k., Kumar, P., Mandal, B., 2014L, Kumar, P., Mandal, B., Dwivedi P., 2014m., Kumar, P., Kumar, P.K., Singh, S. 2014n, Kumar, P. 2013o., Kumar, P., Dwivedi, P. 2015p, Gogia, N., Kumar, P., Singh, J., Rani, A. Sirohi, Kumar, P. 2014q). It is supposed as a metabolic disorder that occurs due to imperfections either in insulin accomplishment, secretion, or both. It is such a disease that can result in solemn problems that ultimately affect human healthiness. In the long term, these may led to micro and macro vascular complications (Mohana *et al.,* 2012). The frequency of type 2 diabetes is growing to epidemic proportions in definite populations and according to one approximation number of cases for diabetic condition that is presently at 171 million is foreseen to reach 366 million by 2030 (WHO, 2006) and this figure is probable to incline to 642 million by year 2040 (Rahelic, 2011). Figures revealed that 86 million adult persons more than one in three U.S. population are with prediabetes influence, which simply means the blood sugar levels of their body are higher than normal level but not so high that are considered as type 2 diabetes, explained by CDC (Centers for Disease Control and Prevention). It is estimated that (2010-2030) the number of adults in developing countries will be increased by 69% and it will be increased by 20% in developed countries (Rizvi *et al.,* 2010, Kumar, P., 2014r., Kumar, P., Dwivedi, P., Singh, P., 2012s, Mishra, P.K., Maurya, B.R., Kumar, Pp. 2012t, Kumar, P., Mandal, B., Dwivedi, P. 2011u. Kumar, P., Mandal, B., Dwivedi, P. 2011v, Kumar, P., Pathak, S. 2016w, Pathak, S., Kumar, P., Mishra, P.K., Kumar, M. 2016x). Moreover, it has been considered that by the year 2030, the mentioned figure will hike to over 366 million and the raise will be particularly observed in developing nations in people age group between 45 to 64 years. Diabetes mellitus (DM) disorder is accompanying by oxidative stress (Rizvi *et al.,* 2010). International Diabetes Federation (IDF) estimated that currently 327 million persons are suffering from this disease, projected to reach 438 million individuals by 2045. Most common form of this disease, Diabetes type 2, which is representing in 90% of the total influenced population. Previous estimates of CDC's based on data from 2010, revealed that 26 million people in the United States are diabetic, and 79 million more are under pre-diabetic conditions. The antidiabetic vegetation used from the Ayurveda times has been extensively recommended for diabetic treatment with less known automatous basis of their working. Easy availability and mild nature of traditional herbal medicines resulted this sector to emerge as an important part of public health service (Rahmam *et al.,* 2013, Kumar, P., Harsavardhn, M. *et al*., 2018y. Kumar, P., Yumnam, J. *et al*., 2018z, Kumar, P., Pandey, A.K., *et al*., 2018aa, Kumar, P., Kumar, S. *et al*., 2018bb, Kumar, P.,

Krishna, V., *et al*., 2018cc, Kumar, P. and Dwivedi, P. 2018gg. Kumar P., Siddique A., *et al*., 2018ff, Kumar, P, Pathak, S, Kumar, M and Dwivedi, P. 2018cd, Kumar P. and Pathak S. 2018kk, Kumar P and Pathak S. 2018pq. Singh *et al* 2020a., Singh *et al*., 2020b., Sood, *et al*., 2020., Bhadrecha *et al* 2020, Singh *et al*., 2020c, Sharma *et al*., 2020, Singh *et al*., 2020d, Bhati *et al*., 2020, Singh *et al*., 2019, Sharma *et al*., 2019).

Types of diabetes

The three different types of diabetes exhibiting different etiology are shown in fig. 1. The type 1 diabetes, also identified as insulin-dependent diabetes mellitus or juvenile diabetes is considered to be an autoimmune disorder condition. Immune system of assaults the islet cells of the pancreas in body, and these cells produce insulin which is the blood-sugar-regulating hormone. Consequently, the pancreas either does not yield insulin, or not sufficient for necessary functions of the body. About 5 per cent of such cases are Type 1 kind, which is generally identified in juvenile stage. Type 1 diabetes is principally the consequently the result of autoimmune devastation of beta cells of the body (Salsali *et al.,* 2006). Normally Type 1 diabetes starts in juvenile phase and in this case pancreas discontinues making of insulin hormone and as consequently one have type 1 diabetes. The connection between family history and risk for diabetes has been well documented as the most common cause of it (Harrison *et al.,* 2003).

The other type of diabetes includes Type 2 diabetes mellitus conditions also known as Non-insulin dependent diabetes mellitus (NIDDM). This is the most communal type of diabetes and constitutes 90% of the diabetic population (Modak, 2015). In this case, the pancreas secretes adequate amount of insulin, but the system of body fails to respond to this hormone. This kind of situation is called insulin resistance. Scientists fail to explain that why some people develop insulin resistance condition and others are normal. Normally due to obesity and under insufficient insulin secretion conditions type 2 diabetes occurs (Salsali *et al.,* 2006). The risk factors of Type 2 are overweight or obesity, decreased glucose tolerance, resistance towards insulin, traditional background. Connected genetic variants linked with the risk of diabetes had an insignificant influence on the ability to suppose the future advancement of type 2 diabetes (Lyssenko *et al.,* 2008).

Gestational diabetes also known as Type 3 diabetes is similar to type 2 diabetes, this disorder occurs when the body fails to respond to insulin hormone. This kind of diabetes starts during pregnancy and in particular cases it may disappears after pregnancy; while it may also become chronic too. The hormonal changes during pregnancy especially high levels of placental hormones are the reason of high blood glucose levels (Lindsay, 2009).

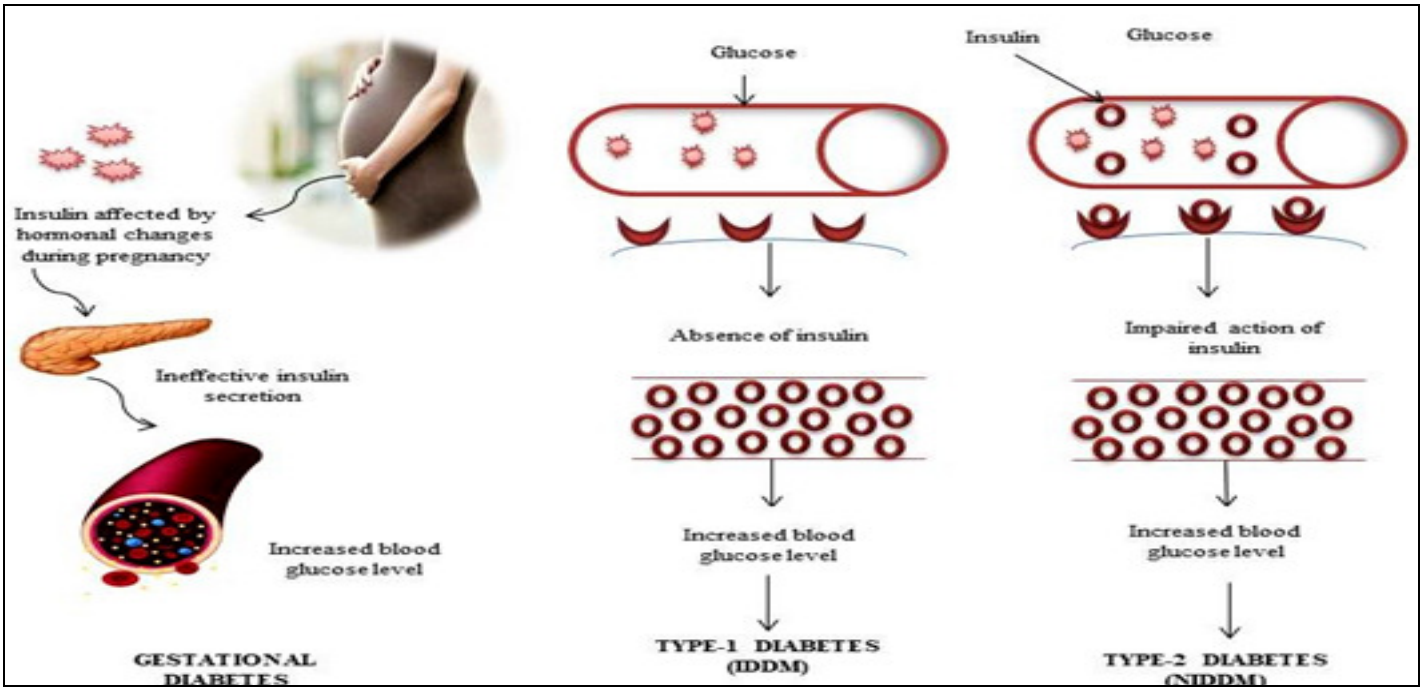

Fig. 1: Pictorial view of types of diabetes mellitus

Complications of Diabetes Mellitus

Chronic hyperglycemia resultant from diabetes brings about an inclination in oxidative anxiety due to more production of reactive oxygen species (ROS) and glucose-protein glycosylation and autoxidation. Production of ROS may result in oxidative damage of some structural components of cells which terminate into complications affecting the nerves, kidney, blood vessels and eyes. Diabetes is regarded as multifactorial disease and the improper management of diabetes causes micro and macrovascular complications like neuropathy, retinopathy and nephropathy (Prabhakar 2016 and Banerjee *et al.,* 2019). If glucose levels in blood are beyond particular range for a long period may result in cataracts and/or retinopathy in the eyes. If not taken care, diabetic nephropathy may result in dysfunctioning, dialysis or sometimes kidney transplantation. Poorly controlled or uncontrolled diabetes may lead failure of the kidneys; not be able to clean the blood appropriately. Diabetic condition can harm body tissues, along with the blood vessels and heart. Two-thirds of people with diabetic case might face heart disease or stroke. Diabetic condition may lead to blindness or harm eyes. Due to this reason diabetic people are instructed to undertake regular eye inspections, so that major eye problems can be prevented.

Diabetes disorder also carries a risk of many other health problems which may include skin problems, damage to the arteries, which may cause reduction in blood flow towards feet. Another complication is impairment of nerves, which makes it hard for people with diabetes to observe wounds, ulcers or blisters, on their feet, that may lead to exclusion. Thus, diabetic people must take care of their feet and pay attention to possible problems. Neuropathy is a complication that results from long span diabetes. Expected mechanisms of neuronal impairment caused by diabetes that are downstream of hyperglycemia and/or forfeiture of insulin signaling include hypoxia, ischemic inflammation and damage of neurotrophic provision. (Daugherty *et al.,* 2018).

To treat all the above-mentioned complications, many hypoglycemic agents are to be used such as metformin sulfonylureas along with glucosidase inhibitors which may lead to severe adverse effects such as diarrhea, diabetic ketoacidosis, and several diabetes complications (Rajalakshmi *et al.,* 2009). It has already been documented that diabetic chronic hyperglycemia is accompanied with dysfunction, long term damage, and ultimately the failure of organs, specially the nerves, blood vessels eyes, heart and kidneys. It also adversely effects lipid, carbohydrate and protein metabolism and may lead to chronic hyperglycemia and irregularity of lipid profile. Such condition may result in series of some further complications including ketosis and polyphasia, even cardiovascular disorder. Although various hypoglycemic agents are used frequently diabetes and the correlated complications endure to be a foremost health problematic issue worldwide and it may affect nearly 10% of the inhabitants all over the world (Burke *et al.,* 2004). Diabetic may suffer from nerve damage because of diabetes, called as diabetic neuropathy. The small sized blood vessels associated with nerves, eventually get damaged and feeding to blood vessels is hampered. There are different forms of diabetic neuropathy viz. focal, autonomic, peripheral, and proximal. One of the most common form is peripheral neuropathy in which nerve damage occurs to the hands and feet. In these circumstances individuals who have had type 2 diabetes from long time and they are not managing their blood glucose levels well, may lose sensation in their feet. Sometimes they may also experience weakness, pain, or tingling like sensation.

Most serious complication of peripheral neuropathy in the feet, a sore on foot. The sore may become infested, the infection can spread, and left unattended, the foot may need to be removed to keep the infection from spreading further. The accessible hypoglycemic agents used for example sulfonylureas, metformin, and glucosidase inhibitors have major adverse effects like diarrhea, diabetic ketoacidosis, and various other diabetes complications (Rajalakshmi *et al.,* 2009). Type 2 diabetes, may also affect the large blood vessels, and may lead to plaque buildup and possibly causing heart attack or vessel blockage in the legs, known as peripheral vascular disease.

Diabetes is a severe metabolic ailment and many medical plants are used to cure diabetes. Nowadays, several kinds of treatments, such as pharmacotherapy, diet remedy, and insulin treatment, are available to regulate diabetic condition. The mechanism of action of glucose lowering drugs include encouragement of insulin secretion by some drugs like sulfonylurea and meglitinides, reduction of hepatic gluconeogenesis by biguanides and postponement in the absorption of carbohydrates from the intestine by alpha-glucosidase (Hui *et al.,* 2005), inclination of peripheral absorption of glucose by thiazolidinediones and biguanides (Bathaie *et al.,* 2012). Regardless of the substantial progress, the consequences are still far from perfection. Such kinds of treatments have some weaknesses like reduction in efficiency and toxicity. For example, sulfonylureas drug may lose their efficiency after a time period of 6 years treatment. It is considered that glucose-lowering drugs are not able to administrate hyperlipidemia conditions (Dey *et al.,* 2002). There are several synthetic medicines developed for diabetic patients, but it has never been described that someone had improved totally from diabetes condition (Li *et al.,* 2004).

In addition, the side effects of such drugs and their interactions with other medicines *in vitro* must be kept in view by medical staff. Today, many kind medicinal plants are recommended for diabetes regulation (Kooti *et al.,* 2015). Such plants execute anti-hyperglycemic effects which have ability to improve working of pancreas organ, hence, increase insulin or reduction in the absorption of glucose.

Role of plants in diabetes

People use a variety of antidiabetic medicines that are available in the pharmaceutical market are insulin secretagogues, insulin sensitizers, inhibitors of intermediary metabolism, and inhibitors of GI glucose absorption and inslinomimetic drugs (Nimesh *et al.,* 2019).

However, these medicines are expensive, and their side effects are problematic (Adegoke and Oloyede, 2013). India is also known as the "botanical garden of the world" as it is rich in biodiversity and more than 70% of rural population reliant on customary plant medicines (Seth & Sharma 2004). Various kinds of medicinal herbs are produced in India and it appears that natural plant wealth of India grasps a key to its conventional wisdom of beneficial herbs. According to one study, more than 80% diabetic patients wish to be treated by herbs as they have lesser side effects (Ezuruike and Prieto, 2016). Especially Himachal Pradesh is blessed with very good plant diversity including various plants which are medicinally useful (Gulati *et al.,* 2004). Previous literature also publicized native information of medicinal species used by public in various parts of the state (Chand *et al.,* 2016). The prospects of consuming the plant as an herbal medicine are vast due to the extensive diversity of plants in the world. Geographical and cultural factors also assisted herbal treatment of several diseases in various formulations like paste of plants, crude extracts, and infusions and as whole plants etc. (Samuelsson, 2006, Marques & Farah 2009). Accessibility and smooth nature of traditional herbal medicines treated this sector an imperative part of public health service/issues (Rahman *et al.,* 2012). Various researches have proved that diabetes condition improving compounds like curcumin, eugenol, etc. are also found in spices crop (Srinivasan, 2006). An extensive assemblage of plant-derived active principles representing numerous bioactive compounds has been recognized for their role for managing diabetes (Patil *et al.,* 2011). Another study has described antidiabetic potential of various vegetables like legumes and cucurbits (Tang *et al.,* 2008). It was revealed that 656 plant species have been used to regulate diabetes and/or been considered good for antidiabetic activity (Simmonds *et al.,* 2006). A list of such medicinal plants with

verified antidiabetic is compiled in table 1 and includes *Neem*, Tulsi, Curry-leaf tree and others.

In the last few years, there has been an emerging interest in the herbal drugs in care and directive of diabetes both in developed and developing nations, due to their natural accessibility and scarcer or no side effects (Hasani-Ranjbar *et al.,* 2009 & Rahimi *et al.,* 2005). Lot of antidiabetic medicines is accessible in market for diabetes and its allied complications; still, presently no effective therapy is accessible to regulate diabetes. The hypoglycemic influence of pharmacologically active constituent of plant reduce the effect on α-amylase and various indirect and direct effects of various blood parameters accountable for advancement of diabetes (Murali, 2006). Biological actions of the plants are associated to chemical composition that are rich in flavonoids, terpenoids, phenolics, alkaloids, glycosides and coumarins, generally show encouraging effects. On the other hand, many conservative drugs for treatment of diabetes, for example metformin are secretagogues which have been originated from a plant (Grover *et al.,* 2002). Metformin is preferred oral blood glucose-lowering agent to regulate type 2 diabetes. A traditional herbal used as medicine in Europe (Galega officinalis - goat's rue, professor weed Italian fitch French lilac or Spanish sainfoin) helped a lot in lower blood glucose. Its derivatives, comprising metformin, were produced and some (not metformin) were used to manage diabetes in the 1920s - 1930s but were discontinued due to toxicity and enhanced the availability of insulin. it is now categorized as a noxious weed in USA (Bailey, 2017).

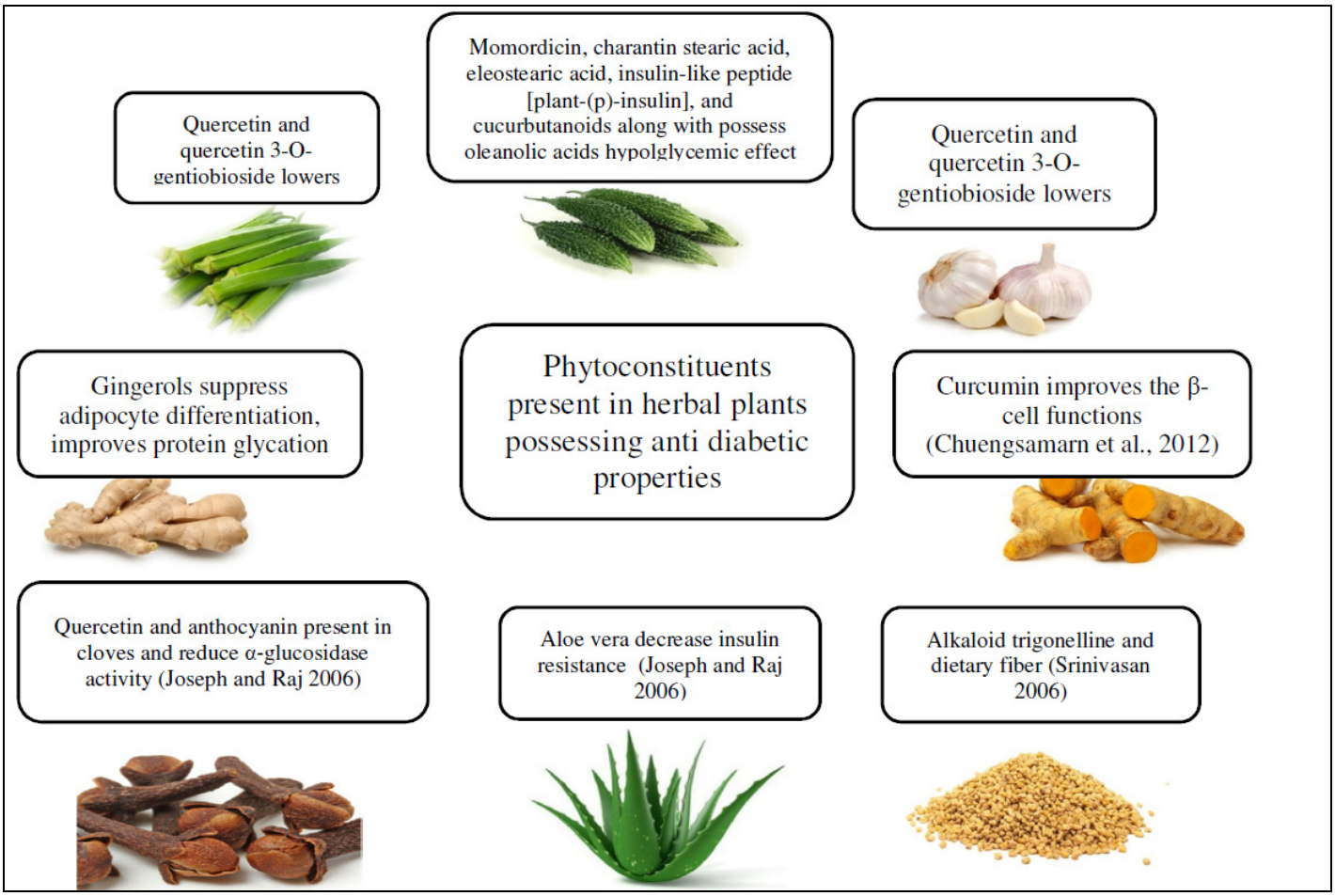

Fig. 2: Adverse reactions and safety of commonly consumed plants for the treatment of diabetes

Table 1: Plants showing anti-diabetic properties and recommended doses

S. No.	Name of plant	Scientific name	Plant part used	Nature of extract	Active chemical constituent	Recommended Dose	Reference
1.	Neem	*Azadirachta indica*	Leaves seeds, bark and root	Aqueous and alcoholic extract	Tetranortriterpenes, Nimbidin	250 mg/kg	Maghrani *et al.,* (2005); Patil *et al.,* (2011)
2.	Jamun	*Eugenia jambolana*	Decoction of kernels	Aqueous and alcoholic extract, lyophilized powder	Glutathione peroxidase, glutathione-s-transferase	-	Jagetia, (2018)
3.	Tulsi	*Ocimum sanctum*	leaves	Ethanolic	Eugenol, polyphenols, caffeic acid, p-coumaric acid	2 gram/kg	Chauhan *et al.,* (2010); Antora and Salleh (2017)

4.	Bael	*Aegle marmelos*	Leaf, Seed, Fruit	Ethanolic Aqueous	Aegeline-2, Coumarin, Flavonoid & Alkaloid	I.p., 14d; p.o., 14d; 1.0 g/kg	Adebajo *et al.,* (2006); Kesari *et al.,* (2006) ;Narendhirakannan *et al.,* (2006)
5.	Mandarin or Mandarine	*Citrus reticulate*	Fruit	Essential oil	Essential oil	500-2000	Fr¨ode *et al.,* (2008)
6.	Curry-leaf tree	*Murraya koenigii*	Leaf, Fruit	Fruit juice	Carbazole, Alkaloid	2.5-5.0 ml/kg	Sharma *et al.,* (2011; Makheswari *et al.,* (2012)
7.	Garlic	*Allium sativum*	Root	Ethanolic	Ajoene,Diallyl disulphide oxide, Allyl propyl disulphide, S-allyl mercaptocysteine, S-allyl cysteine	P.o., 14d, 21-112 d	Eidi *et al.,*(2006), Tanaka *et al.,* (2006) Makheswari *et al.,* (2012)
8.	Guava	*Psidium guajava*	Leaf, Fruit	Aqueous, Methanolic	Terpen, Flavonoid, Strictinin, Isostrictinin, Pedunculagin	P.o., AT; 100-400 mg/kg	Musabayane *et al.,* (2005), Chauhan *et al.,* (2010)
9.	Bitter melon	*Momordica charantia*	Whole plant	Methanolic, Aqueous, chloroformic	Lectin Charantin, Momordicin, Galactose binding, β-sitosterol Diosgenin, Cholesterol, lanosterol, Cucurbitacin glycoside	p.o., 27-30d; 10-20 mg/	Saxena *et al.,* (2004), Shetty *et al.,* (2005), Sathishsekar *et al.,* (2005)
10.	Kaarali-kanda	*Momordica*	NA	NA	Steroidal glycoside or phenolics	0.5g/kg	Harinantenaina *et al.,* (2006)
11.	Mango tree	*Mangifera indica*	Leaf, Bark Stem, Fruit	Aqueous, Alcoholic	Mangiferin, Flavonoid Phenolics etc.	i.p., AT; 100-200 mg/kg	Ojewole *et al.,* (2005) and Prakash *et al.,* (2005)
12.	Barbados aloe	*Aloe vera*	Leaf	Ethanolic	Pseudoprototinosaponin, Prototinosaponin	P.o., 28d	Ayodhya *et al.,* (2010) and Fr¨ode *et al.,* (2008)
13.	Papaya	*Carica papaya*	Fruit	Aqueous	Saponin, Tannin, Alkaloid, Flavonoid	100-400	Sharma *et al.,* (2011)
14.	Bhindi	*Abelmoschus esculentus*	Fruit	Ethanolic	Carbohydrate Gum, Mucilage, Protein Volatile oil, Phenolics, Phytosterol, Flavonoid, Tannin	300	Sharma *et al.,* (2011)
15.	Pomegranate	*Punica granatum*	Fruit	Ethanolic	Tannin	P.o., 200	Sharma *et al.,* (2011)
16.	Terminalia chebula	*Chebulic myrobalan*	Seed, Fruit	Chloroform, Aqueous	Shikimic, Gallic, Triacontanoic, Palmitic acid, β-sitosterol, Daucosterol	p.o., AT; 200 mg/kg	Eddouks *et al.,* (2005); Lo *et al.,* (2006), Abdel-Zaher *et al.,* (2005)
17.	Ginger	*Zingiber officinale*	Root	Ethyl acetate	Gingerols, Shoagols		Suhani & Khatua (2018) Rani *et al.,* (2011)
18.	Turmeric	*Curcuma longa*	Root	Ethanol and/or hexane extraction	Curcumin		Suhani & Khatua (2018)
19.	Fenugreek	*Trigonella foenum*	Seeds, husk and cotyledons		Saponin, Protein and Polyphenols	10 grams of fenugreek seeds soaked in hot water	Naidu *et al.,*(2010)
20.	Cloves	*Syzygium aromaticum*	EtOH extract of clove	50% aqueous	extracts of clove, eugeniin		Sanae *et al.,*(2014)

Mechanism of action of antidiabetic property in medicinal plants

The actions are described by processes like inhibiting renal glucose absorption, reducing insulin resistance and stimulating insulin secretion from beta cells. The mechanism also includes inhibition of insulin degradative processes and repairment of damaged pancreatic beta cells (Oyagbemi *et al.,* 2014). Improving insulin production and stimulation of the process of glycogenesis and hepatic glycolysis by the herbal plants has been reported (Esmaeili & Yazdanparast, 2004). The mechanism of action for the anti-diabetic potential of medicinal plants includes stimulation of insulin production and secretion from beta cells of islets, inhibition of insulin degradative processes, inhibition of renal glucose reabsorption and reduction in insulin resistance (Mukherjee *et al.,* 2006), repairing pancreatic beta cells with increasing

the size and number of cells in the islets of Langerhans (Mohamed *et al.,* 2006). Esmaeili & Yazdanparast, (2004) stated that insulin secretion and glycogenesis and hepaticglycolysis are stimulated by the compounds present in medicinal plants (Miura *et al.,* 2001). It was also reported that the conversion of starch into glucose and inhibitory mechanism of β-galactocidase, α-glucocidase and alpha-amylase also lowers the cortisol level (Heidari *et al.,* 2005). The antidiabetic activity of medicinal plants due to the possession of antioxidant activity which are also involved in treating the dysfunctioning of pancreatic β-cell by decreasing the oxidative stress load has been documented by Kaneto *et al.,* (2005). Furthermore, there are many kinds of glucose-depressing medicines that employ anti-diabetic influences through several procedures. These approaches comprise encouragement of insulin discharge by meglitinides and sulfonylurea medicines, inclination of peripheral preoccupation of glucose by thiazolidinediones and biguanides (Bathaie *et al.,* 2012), postponement in the absorption of starches etc. from the digestive system by alpha-glucosidase, and diminishing of hepatic gluconeogenesis by biguanides (Hui *et al.,* 2005).

Safety and Toxicity of herbal medicines

The allergic compounds present in many ordinary foods are alpha gliadin produced by gluten in wheat, oats and rye, the cyanogenic glycosides in many fruit seeds, alkaloids of the Solanaceae and lectins of many pulses including soya and red kidney beans and the thiocyanates of the Brassica vegetables. The phytoconstituents present in plant like flavonoids, alkaloids and other antioxidants possess antidiabetic properties as shown in fig. 2. The alkaloids present in plants inhibit the action of alpha-glucosidase and reduces the transport of glucose through intestinal epithelium. Similarly, polysaccharides increase the level of insulin and improve glucose tolerance. Flavonoid helps in reducing the glucose levels by stimulating the function of hepatic glucokinase. Dietary fibers present in plant reduces glucose diffusion and suppress the action of alpha-amylase (Parikh *et al.,* 2014).

The efficacy of the leaves and fruits of medicinal plants, including boar (*Zizyphus jujuba*) and jambhul (*Eugenia jambolana*) for the treatment of diabetes, investigation regarding the presence of elements such as Hg, Ni, Cr, Pb, and Cd was conducted. The study revealed the presence of various investigated elements because of the environmental pollution. Subramanian *et al.* (2012) studied the presence of Na, Mg and Mn in various medicinal plants used for the preparation of Indian curries and they reported that plants such as pudina, siru keerai and pulicha keerai were the excellent source of essential elements that are beneficial to human health. These plants can be the excellent component for treating the diabetic population for lowering the blood glucose level (Eluid *et al.,* 2012).

Need for regulatory controls on herbal drugs

Herbal drugs are defined by those traditional medicines which are prepared solely from medicinal plant preparations for therapy. WHO has also defined the concept of traditional medicine that have been in existence from almost several hundreds of years before the development of modern medicine. The FDA Modernization Act and *European* Agency for the Evaluation of Medicinal *European* Union Products has taken keen interest for formulating the regulatory frameworks for governing the botanical drugs which is more important for the markets for the formulation of herbal drugs within the set limits (Sinha *et al.,* 2014).

Herb-drug interactions

The pharmacological or chemical interactions are caused due to the administration of two or more drugs together which further changes the effect of the agents and leads to the either increase or decrease in effectiveness or severity of adverse effects. The co-administration of pharmaceutical agents and antidiabetic herbs causes herb-drug interactions which leads to enhanced effects or adverse drug events like hypoglycemia (Gupta *et al.,* 2017).

Advantages of herbal plants over diabetic drugs

The need of herbal medicines also termed as *phytomedicine*, for the treatment of diabetes is highly needed as the future of orally active botanical substitute for insulin is lagging behind. The requirement for new molecules for the stimulation of endogenous insulin biosynthesis and secretion are realistic possibilities. The side effects caused by insulin therapy and oral hypoglycemic drugs increased the demand of more safe and effective antidiabetic drugs (Bolen *et al.,* 2007). The herbal medicine could be the useful source of new oral hypoglycemic compounds for future development either as dietary adjuncts of pharmaceutical entities for treating diabetes mellitus as they could produce maximum therapeutic efficacy with less side effects (Farag *et al.,* 2014).

Limitations of herbal plants use

Despite of all the medicinal properties of the herbal plants documented in many studies, the evidence for clinical trials is still lacking in the scientific world. Though the market value of herbal medicine is increasing day by day with inadequate regulations but the evidence-based data is missing. Henceforth, need of standardization, safety, efficacy, risks/benefits along with the adverse reactions associated with the overuse of the herbal plants is absolutely required (Farag *et al.,* 2014). However, plants become toxic when targeted by pathogens like bacteria or fungi and produces toxic phytochemicals and phytoalexins. These phytochemicals are responsible for cancer growth and can cause severe gastrointestinal or allergic problems (Makheswari & Sudarsanam 2012). Moreover, 'herbal' medications have been contaminated with therapeutic chemicals that were withdrawn due to some serious contrary proceedings. In Singapore, screening 2000 (almost) Chinese proprietary drugs exhibited that a preparation marketed as 'Wonder pills' for regulating diabetes mellitus contained the withdrawn chemical phenformin (Koh & Woo 2000). In the past three centuries, regardless of the noteworthy advancement made in the regulation of diabetes, the results of such application in patients is still far away from perfection. These kinds of treatments have some drawbacks, comprising drug confrontation (lessening of proficiency), some side effects, and also poisonousness. For instance, some anti-diabetic drugs like sulfonylureas may lose their efficiency after 6 years of application in 44% patients. Moreover, the side effects of drugs and interactions with each other in vitro must be deliberated. Currently, several treatments that include the use of plants having herbal properties are suggested (Kooti *et al.,* 2015). There are a several challenges associated with use of herbal medicine like very little information about active constituents of the

same (Brantley *et al.,* 2014), lack of thorough product information (Neergheen, 2013 and Kunle *et al.,* 2012), complication due to manifold chemical components (Bensoussan *et al.,* 2015), difference in source of herbal product, lack of calibration like processes and batch–lot reproducibility (Ip *et al.,* 2010 and Arun *et al.,* 2012) and of documentation of genuineness of herbs used in production procedure (Kalyankar *et al.,* 2014 and Flower *et al.,* 2014). Furthermore, the existing scientific indication, mainly clinical, to provision the use of herbal medicine remnants at the lesser levels, and the heftiness of the methods used has often been insufficient (Chavez *et al.,* 2006, Del Prete *et al.,* 2012 and Ge *et al.,* 2014).

Conclusion

The foremost purpose of this review paper is to familiarize a number of effective medicinal plants used, effectively and for economical treatment of diabetes. However, such kind of the secondary effects of these treatments (e.g., hepatotoxicity and gastrointestinal disorders), have resulted in accessing natural alternatives for diabetic patients. According to available outcomes, it may be supposed that medical plants are inexpensive and having fewer or no side effects in comparison to synthetic drugs. An attempt has been made to examine the antidiabetic plants and it may be beneficial to research scholars, scientists, and professionals working in the field of therapeutics and pharmacology to develop antidiabetic drugs. Many prevailing medicines are derivative of these plants. Therefore, regulating diabetes with plant extraction which are accessible and do not require laborious pharmacological synthesis seems highly attractive.

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Conflict of interest

Authors declare that there is no conflict of interest between them.

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